B1 cont

7. (AMENDED) The signal amplification system as claimed in claim 1, wherein the modulating substance is a natural activator, or a fragment thereof, of the enzyme.

C1 B2

10. (AMENDED) A method of selecting a molecule of interest which is capable of binding to target ligand wherein the interaction between the said molecule of interest and the said target ligand is detected with a signal amplification system as claimed in claim 1, by means of generating a signal amplification and triggering transcriptional activation.

13. (AMENDED) The method of selecting a molecule of interest as claimed in claim 10, wherein the signal amplification system comprises a bacterial multi-hybrid system of at least two distinct fragments of an enzyme, whose enzymatic activity is restored by the interaction between the said molecule of interest and the said target ligand.

B3 sub C2

14. (AMENDED) The method of selecting a molecule of interest as claimed in claim 10, wherein the signal amplification system comprises bacterial multi-hybrid system of at least a first fragment of an enzyme and a modulating substance, whose activity is restored by the interaction between the said molecule of interest and the said target ligand.

15. (AMENDED) The method of selecting a molecule of interest as claimed in claim 10, wherein the target ligand is selected from the group consisting of protein, peptide, polypeptide, receptor, ligand, antigen, antibody, DNA binding protein, glycoprotein, lipoprotein and recombinant protein.

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16. (AMENDED) The method of selecting a molecule of interest as claimed in claim 10, wherein the molecule of interest is capable of interacting with the target ligand and optionally of binding to said target ligand.

17. (AMENDED) The method of selecting a molecule of interest as claimed in claim 10, wherein the interaction between the molecule of interest and the target ligand is detected, by means of signal amplification which triggers transcriptional activation, and is quantified by measuring the synthesis of the signaling molecule or the expression of the reporter gene.

21. (AMENDED) The method of selecting a molecule of interest as claimed in claim 10, wherein the molecule of interest is a mutant molecule compared to the known wild type molecule and said molecule of interest is tested for its capacity of interacting with the target ligand.

22. (AMENDED) The method of selecting a molecule of interest as claimed in claim 10, wherein the selection is performed in an *E. coli* strain, or in any bacterial strain deficient in endogenous adenylate cyclase or any other eukaryotic cell.

23. (AMENDED) A kit for selecting molecule of interest, wherein said kit comprises:

(A) a signal amplification system as claimed in claim 1;

(B) an *E. coli* strain, or in any bacterial strain deficient in endogenous adenylate cyclase or any other eukaryotic cell and;

(C) a medium allowing the detection of the complementation selected from the group consisting of indicator or selective medium as minimal medium supplemented with lactose or maltose as unique carbon source, medium with antibiotics, medium to

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visualize fluorescence, conventional medium and medium which allows the sorting by the presence of the phage receptor.

24. (AMENDED) A kit for selecting a molecule of interest, wherein said kit comprises:

(A) a signal amplification system as claimed in claim 1 wherein the molecule of interest is a mutant molecule compared to the known wild type molecule and the known wild type molecule of interest is the control;

(B) *E. coli* strain, or in any bacterial strain deficient in endogenous adenylate cyclase or any other eukaryotic cell and;

(C) a medium allowing the detection of the complementation selected from the group consisting of indicator or selective medium as minimal medium supplemented with lactose or maltose as unique carbon source, medium with antibiotics, medium to visualize fluorescence, conventional medium and medium which allows the sorting by the presence of the phage receptor for each signal amplification system;

(D) means for detecting whether the signal amplification system with the mutant molecule is enhanced or inhibited with respect to the signal amplification system with wild type.

25. (AMENDED) A method of screening for a substance capable of stimulating or inhibiting the interaction between a target ligand and a molecule of interest wherein respectively the stimulating or the inhibiting activity is detected with a signal amplification system as claimed in claim 1, by means of generating an amplification and respectively of triggering or of abolishing transcriptional activation, and wherein said signal amplification and said triggered or abolished transcriptional

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activation are compared with those obtained from an identical signal amplification system without any substance.

28. (AMENDED) The method of screening for a substance capable of stimulating the interaction between a target ligand and a molecule of interest as claimed in claim 25, wherein the signal amplification corresponds to the production of a signaling molecule.

29. (AMENDED) The method of screening for a substance capable of inhibiting the interaction between a target ligand and a molecule of interest as claimed in claim 25, wherein the signal amplification corresponding to the production of a signaling molecule is blocked or partially abolished.

30. (AMENDED) The method of screening for a substance capable of stimulating the interaction between a target ligand and a molecule of interest as claimed in claim 25, wherein the transcriptional activation leads to a reporter gene expression.

31. (AMENDED) The method of screening for a substance capable of inhibiting the interaction between a target ligand and a molecule of interest as claimed in claim 25, wherein the transcriptional activation leading to a reporter gene expression is blocked or partially abolished.

32. (AMENDED) The method of screening for a substance capable of stimulating or inhibiting the interaction between a target ligand and a molecule of interest as claimed in claim 25, wherein the target ligand is selected from the group consisting of receptor, ligand, antigen, antibody, DNA binding protein, glycoprotein and lipoprotein.

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33. (AMENDED) The method of screening for a substance capable of stimulating or inhibiting the interaction between a target ligand and a molecule of interest as claimed in claim 25, wherein the substance is selected from the group consisting of protein, glycoprotein, lipoprotein, ligand and any other drug having stimulating or inhibitory affinity.

34. (AMENDED) The method of screening for a substance capable of stimulating or inhibiting the interaction between a target ligand and a molecule of interest as claimed in claim 28, wherein the signaling molecule corresponds to the synthesis of cAMP.

35. (AMENDED) The method of screening for a substance capable of stimulating or inhibiting the interaction between a target ligand and a molecule of interest as claimed in claim 28, wherein the signaling molecule corresponds to the synthesis of cGMP.

36. (AMENDED) The method of screening for a substance capable of stimulating or inhibiting the interaction between a target ligand and a molecule of interest as claimed in claim 30, wherein the reporter gene expression is selected from the group consisting of gene coding for nutritional marker such as lactose, maltose; gene conferring resistance to antibiotics such as ampicillin, kanamycin or tetracyclin; gene encoding for toxin; color marker such as fluorescent marker of the type of the Green Fluorescent Protein (GFP); gene encoding for phage receptor proteins or fragment thereof such as phage λ receptor, *lamB* and any other gene giving a selectable phenotype.

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37. (AMENDED) The method of screening for a substance capable of stimulating or inhibiting the interaction between a target ligand and a molecule of interest as claimed in claim 25 [to 36], wherein the molecule of interest is a mutant molecule compared to the known wild type molecule and said molecule of interest is tested for its capacity of interacting with the target ligand.

38. (AMENDED) The method of screening for a substance capable of stimulating or inhibiting the interaction between a target ligand and a molecule of interest as claimed in claim 25, wherein the screening is performed in an *E. coli* strain, or in any bacterial strain deficient in endogenous adenylate cyclase or any other eukaryotic cell.

39. (AMENDED) A kit for screening for a substance capable of stimulating or inhibiting the interaction between a target ligand and a molecule of interest, wherein said kit comprises:

(A) a signal amplification system as claimed in claim 1 with the substance capable of stimulating or inhibiting the interaction between a target ligand and a molecule of interest, without any substance as the control;

(B) *E. coli* strain, or in any bacterial strain deficient in endogenous adenylate cyclase or any other eukaryotic cell and;

(C) a medium allowing the detection of the complementation selected from the group consisting of indicator plate or selective medium as minimal medium supplemented with lactose or maltose as unique carbon source, medium with antibiotics, medium to visualize fluorescence, conventional medium, and medium which allows the sorting by the presence of the phage receptor and;

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(D) means for detecting whether the signal amplification system with the substance is enhanced or inhibited with respect to the signal amplification system without any substance.

40. A molecule of interest identified by the method of claim 10.

41. (AMENDED) A molecule of interest corresponding to a polynucleotide capable of expressing a molecule which interacts with a fused target ligand coupled with an enzyme or a fragment thereof.

42. (AMENDED) A substance capable of stimulating or inhibiting the interaction between a target ligand and a molecule of interest identified by the method as claimed in claim 25.

43. (AMENDED) The signal amplification system as claimed in claim 1, wherein the bacterial multi-hybrid system contains:

(A) a first chimeric polypeptide corresponding to a first fragment a of an enzyme;

(B) a second chimeric polypeptide corresponding to a second fragment of an enzyme or a modulating substance capable of activating said enzyme and;

(C) a substance capable of stimulating or inhibiting the interaction between a target ligand and a molecule of interest, wherein the first fragment is fused to a molecule of interest and the second fragment or the modulating substance is fused to a target ligand and wherein the activity of the enzyme is restored by the interaction between the said molecule of interest and the said target ligand and wherein a signal amplification is generated.

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44. (AMENDED) A polynucleotide sequence coding for the signal amplification system as claimed in claim 1, wherein the polynucleotide sequence codes for a bacterial multi-hybrid system of at least two chimeric polypeptides containing:

(A) a first chimeric polypeptide corresponding to a first fragment a of an enzyme fused to a molecule of interest;

(B) a second chimeric polypeptide corresponding to a second fragment of an enzyme or a modulating substance capable of activating said enzyme fused to a target ligand.

45. (AMENDED) A polynucleotide sequence coding for the signal amplification system as claimed in claim 1, wherein the polynucleotide sequence codes for a bacterial multi-hybrid system containing:

(A) a first chimeric polypeptide corresponding to a first fragment a of an enzyme fused to a molecule of interest;

(B) a second chimeric polypeptide corresponding to a second fragment of an enzyme or a modulating substance capable of activating said enzyme fused to a target ligand;

(C) a substance capable of stimulating or inhibiting the interaction between a target ligand and a molecule of interest.

IN THE SPECIFICATION:

Please amend the specification as follows:

On page 30, please replace the first paragraph with the following paragraph:

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